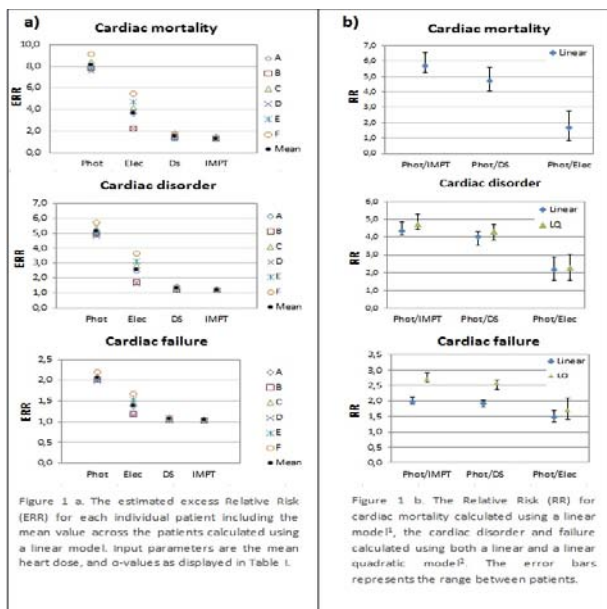


defined as the ratio between ERR for photon /electron, photon/DS and photon/IMPT.

Table I: Dose-response models, parameters and 95 % CI

	Model	Parameter	95 % CI
Mortality	Linear ¹	$\alpha: 0.6$	0.2; 2.5
Disorder	Linear ²	$\alpha: 0.35$	-0.005; 1.2
	LQ	$\alpha_1: 0.4$	0.002; 1.4
		$\alpha_2: -0.00013$	-0.01; 0.1
Failure	Linear ²	$\alpha: 0.09$	-0.02; 0.3
	LQ	$\alpha_1: 0.19$	-0.02; 0.5
		$\alpha_2: -0.002$	-0.004; 0

Results: Regardless of dose-risk model applied, the conformal photons were ranked with the highest ERR for all cardiac toxicities, whereas IMPT was ranked with the lowest (Figure 1a). For cardiac mortality the ERR for photon was 8.1 (95 % CI: 3.4 to 30.5), while ERR for IMPT were 1.3 (95 % CI: 1.1 to 2.4). For cardiac disorder and cardiac failure the ERR for photon was 5.1 (95 % CI: 0.9 to 15.2) and 2.1 (95 % CI: 0.8 to 4.6), respectively (Linear model). The corresponding results for IMPT were 1.2 (95 % CI: 1.0 to 1.7) and 1.1 (95 % CI: 1.0 to 1.2). Similar trends were found using the LQ model. Relative to IMPT, photons lead to a risk of cardiac mortality that was a factor of 6.1 higher (range 5.7 to 7.0), cardiac disorder a factor of 4.3 higher (range 4.1 to 4.9) and cardiac failure a factor of 2.0 higher (range 1.9 to 2.1) (Figure 1b).



Conclusion: Across different cardiac morbidity endpoints, and despite different dose-risk models used, the results of our modelling study were consistently in favour of protons.

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Symposium: Emerging biomarkers

SP-0401

Circulating tumour cells as biomarkers in lung radiotherapy

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It has long been hypothesized that the propagation of circulating tumour cells (CTCs) is a pre-requisite for the development of metastases. However, robust technology to reliably isolate CTCs and characterise them at the molecular level has only become available in recent years. Thus repeated blood sampling for CTCs could provide a non-invasive method of serially reassessing tumour status and evolving tumour biology.

Patients with stage I-III NSCLC are at high risk of developing distant metastases after radiotherapy (RT) or chemoradiotherapy treatment. With the advent of new technologies to enumerate CTCs, the clinical significance of CTCs before, during and after RT has become of great interest. In the current era of targeted therapy and the development of personalised medicine the question still remains as to whether CTCs could be used to identify patients most likely to benefit from radical RT and prevent the delivery of futile cancer treatments and their associated toxicity. Prospective clinical trials have shown the prognostic value of CTC enumeration in patients with non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) (1, 2). Although CTCs have been used as a surrogate biomarker in hundreds of clinical trials, as yet none have been incorporated into standard clinical practice. To date there are few published studies evaluating CTC's in patients undergoing radical thoracic RT.

In my talk I will discuss the following:

- novel platforms available for isolation of CTCs
- current data on the evaluation of CTCs as a biomarker in NSCLC and SCLC patients treated with RT
- advantages and limitations of CTCs as a biomarker
- future directions and the prospect of using CTCs to stratify patients in clinical trials

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SP-0402

The fall and rise of predictive radiotherapy biomarkers

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Radiotherapy is a mainstay of cancer treatment. Due to its high efficacy to inactivate cancer stem cells in the primary tumor and regional metastases as well as its increasing ability to spare normal tissues, it has a proven curative potential in

many cancer types. State-of-the-art radiation treatment planning and delivery is fully individualized based on anatomical imaging, precise space-resolved radiation dose models, tumor control probability- vs. normal tissue complication-models and clinical parameters. These advances in personalized radiation oncology can mainly be attributed to the revolutionary progress in high-precision radiation delivery and planning technology during the past decades and have been rapidly translated into clinical practice. In parallel radiobiological knowledge has significantly improved during the past decades by e.g. unravelling radiobiological mechanisms of radioresistance of tumors and volume-dose relationships for a host of radiation induced effects in normal tissues. This research translated into more efficient radiation schedules on a population base and to NTCP parameters clinically used for treatment planning in individual patients. While several bioassays, including SF2 and plating efficiency determined in human tumor biopsies, provided proof-of-concept of radiobiological mechanisms, these early assays could not be applied to tailor a treatment strategy for an individual patient. Revolutionary advances in biotechnology and tumor biology allow to profile tumors rapidly, thereby providing information on resistance parameters (e.g. hypoxia, stem cell density, radiosensitivity) which can be rationally tested for their prognostic and predictive power for radiotherapy. The same applies for biological imaging which may be of particular relevance for advancing biology-driven individualization of radiation oncology. One uniqueness for the development of personalized radiation oncology is that already a broad biological stratification of patients can substantially enhance individualization as this information adds to the fully anatomically-personalized dose-distributions achieved today. Therefore biomarker driven high precision radiotherapy is in pole position to create a show-case for personalized oncology at large.

This lecture will review preclinical and clinical-translational examples of potential strategies to further personalize radiation oncology by inclusion of biomarkers.

SP-0403

Genomic breast cancer subtype classification for response prediction

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The advent of genomics has revolutionized our understanding of breast cancer as several biologically and molecularly distinct diseases. New molecular techniques generate data about the intrinsic characteristics of a tumour, thereby providing useful diagnostic, prognostic and predictive information. Commercially available tests have begun to fundamentally change the clinicopathological paradigm of selecting patients for adjuvant systemic therapies in early breast cancer. Several recently published radiosensitivity gene expression signatures aim to predict response to adjuvant radiotherapy. The ultimate aim of biomarker research is to individualise therapies in order to maximise tumour response whilst minimizing overtreatment and toxicities. This talk will review the strengths and limitations of currently available breast cancer-specific molecular tests with a view to response prediction.

SP-0404

Genomic subtypes in prostate cancer and its influence in treatment response

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Abstract not received

Symposium: SBRT for oligometastatic disease

SP-0405

Combining SBRT and immunotherapy: a promising approach?

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Clinical reports of limited and treatable cancer metastases, a disease state that exists in a transitional zone between localized and widespread systemic disease, have been reported and are now termed oligometastasis. SBRT treatment of oligometastases has shown promising local control rates (65-97%), and a good toxicity profile (<5% of serious adverse events) because the delivered doses are ablative and spatially limited.^{1, 2} However, most of these patients usually recur at distant sites, outside of the irradiated area, with a median time to progression of 4 to 6 months, indicative of occult metastatic deposits at the time of treatment. Thus, although SBRT is effective in definitively ablating most treated lesions, distant tumors progress highlighting the need for better systemic therapies.³ Immunotherapy has emerged as an independent therapeutic modality that can result in objective - even complete - responses and significant amelioration of overall survival in patients with advanced metastatic tumors. There is an emerging opportunity for combining immune therapy together with ablative SBRT for oligometastatic patients, with the final aim of increasing T cell infiltration into the tumor.

In situ vaccination during lethal RT of few metastases

Lethal (high) doses of radiation can induce immunogenic death in cancer cells, i.e. irradiated cancer cells can trigger an antitumor immune response. RT can upregulate the necessary "eat-me" signals that promote the uptake of dying tumor cells by dendritic cells (DCs) and macrophages⁴. However, a systemic immune response against distant lesions (the so-called abscopal effect) is rarely seen. Given the beneficial but limited immune modulatory effects of SBRT, combination of SBRT with simultaneous activation of other immune-pathways could lead to antigen-specific adaptive immunity, a phenomenon called "*in situ* vaccination".⁵ An abscopal effect has been observed when RT was combined with immunotherapy and has been proven to be T-cell mediated.⁶⁻⁸ A recent report of patients with melanoma and renal cell carcinoma treated with SBRT (20 Gy), in combination with IL-2 showed higher than expected abscopal responses.⁹ In a phase I trial combination 8 Gy in 2-3 fractions with ipilimumab partial responses were observed in 18% of the patients. When dual checkpoint blockade with both anti-CTLA4 and anti-PD-1 combined with radiation was tested in a B16 melanoma model improved responses and abscopal effects were observed. Even in the presence of dual checkpoint blockade, omission of radiation resulted in high rates of relapse.¹⁰

The combination of lethal SBRT to few tumor deposits in combination with different immunotherapy strategies triggers antitumor immunity. However, the key question that needs to be answered is which are the best combinatorial strategies, the best timing to combine them and how to increase effective homing of antitumor T cells to the remaining tumor deposits. Modifying the tumor microenvironment in these residual tumors is therefore of major importance to improve therapeutic outcome and finally cure.

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